REMARKS

Claims 16-29 and 31-44 were pending. Claims 17-22, 27 and 42 were canceled without prejudice. Applicants expressly reserve the right to pursue the subject matter of the canceled claims in related applications. Claims 16, 23-26, 28-29, 31-41, and 43-44 are pending. No claim is allowed.

Summary of Examiner Interview

Applicants gratefully acknowledgement the participation of Examiners Ware and Naff in the interview of December 1, 2004. The lidocaine data and its relevance to the outstanding obviousness rejection were discussed. Applicants reviewed the data showing that lidocaine effectively treated direct lung injury, but had no effect on indirect lung injury and discussed its relevance to the distinct biological sequelae of the two types of injuries. Examiner Naff asserted that the structure and function of lidocaine were too different from the anti-IL-8 antibody to make such a prediction. The Examiner also asserted that it is predicted that IL-8 cytokine is produced in indirect lung injury because it was known that IL-8 was induced in direct lung injury. Thus, according to the Examiner, the treatment of these lung injuries would be expected to be the same.

Objection to the claims

Claims 17-22 are objected to under 37 C.F.R. § 1.75 (c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. According to the Examiner, these claims do not further limit a process for producing a therapeutic agent because they are directed to a method of using and not a method of making *per se*. Applicants traverse this objection.

Claims 17-22 are canceled herein, rendering the rejection moot.

In view of the above, the basis for the objection may be removed.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 27 and 42 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. According to the Examiner, claims 27 and 42 lack antecedent basis for the recitation of "the constant region." Applicants traverse this rejection.

Claims 27 and 42 are canceled herein, rendering the rejection moot.

In view of the above, the basis for the rejection may be removed.

Rejection Under 35 U.S.C. § 102 (a)

Claims 16-29 and 31-44 are rejected under 35 U.S.C. § 102 (a) as allegedly being anticipated by Yokoi et al.. The Examiner alleges that Yokoi teaches processes for producing anti-IL-8 antibody and treatment of hypoxemia. Applicants traverse this rejection.

Applicants respectfully submit that Yokie is not a proper reference under 35 U.S.C. § 102 (a). The earliest priority date for the instant application is July 26, 1996 and September 22, 1996, the filing dates of Japanese patent applications. As the earliest of these dates pre-dates the Yokoi reference, it is not available as a § 102 (a) reference. The specification is amended herein to reflect the priority claim of the instant application.

In view of the above, the basis for the rejection may be removed.

Rejection Under 35 U.S.C. § 103 (a)

Claims 16-29 and 31-44 are rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Folkesson in view of Slotmann for reasons of record. Briefly, the Examiner maintains that "to treat indirect injury or direct injury is clearly an obvious modification of the cited prior art." The Examiner dismisses the submitted abstracts of Nishina and Mikawa, asserting that lidocaine is an entirely different drug than the anti-IL-8 antibody. Applicants traverse this rejection.

Applicants respectfully submit that the combination of Folkesson and Slotmann fail to render the claimed methods *prima facie* obvious for reasons of record as well as those discussed below.

As a preliminary matter, Applicants note that one of skill in the art does *not* equate the direct lung injury model disclosed in Folkesson with the indirect lung injury of the instant claims. Objective evidence already of record demonstrates that the skilled artisan views the direct lung injury and indirect lung injury as *distinct* pathological entities. *See* Bemard et al., *Am J. Respir. Crit. Care. Med.* 146:818-24 (1994) (classifying direct injury and indirect injury separately); *Anesthesiology* Abstracts of Nishina and Mikawa (demonstrating that a therapeutic agent successfully treats direct injury while having no effect on indirect injury). More particularly,

Folkesson discloses IL-8 as a potential target to modulate direct injury because of the neutrophil recruitment to the lungs. *See* Folkesson at 107. However, reports in the literature indicate that indirect injury can occur in patients with severe neutropenia, suggesting that neutrophils may not play a significant role (if any) in indirect injury. *See* Exhibit A. To date, the Examiner has provided no objective evidence (known at the time of filing) to the contrary, *i.e.*, no evidence that direct injury and indirect injury were viewed as asserted by the Examiner. Applicants respectfully request that if the Examiner's rejection is based on facts within her personal knowledge, the Examiner will support this rejection with those facts in an affidavit by the Examiner according to MPEP § 2144.03. According to MPEP § 2144.03,

> When a rejection is based on facts within the personal knowledge of the examiner, the data should be stated as specifically as possible, and the facts must be supported, when called for by the applicant, by an affidavit from the examiner.

Applicants respectfully submit that the cited combination fails to render the claimed methods obvious because the combination fails to teach each and every element of the claimed invention. MPEP § 2143.03. Specifically, the cited combination fails to teach the use of anti IL-8 antibody to treat indirect injury. Folkesson discloses only direct injury, and Slotmann teachings fail to cure this deficiency. In disregarding the objective evidence already on record, the Examiner has not provided any scientific rationale or evidence that suggests a person of skill in the art considered indirect injury and direct injury so closely linked that the treatment of one can be reasonably expected to treat the other. The Abstracts already of record demonstrate that at least one therapeutic agent has completely distinct effects in the treatment of direct injury and indirect injury. While the structure and mechanism of action of lidocaine is different from that of the anti-IL-8 antibody, these differences alone do not render this data irrelevant. The lidocaine has the same mechanism of action in both indirect injury and direct injury, but achieves *different* results. Contrary to the Examiner's position, a person of ordinary skill in the art would interpret this data to suggest that direct injury and indirect injury are *distinct* pathological diseases that ultimately result in lung damage in view of the *different* results achieved using a single therapeutic agent. This is not surprising given the distinct nature of the initiators of direct injury and indirect injury. *See* Exhibit A. If one disease is distinct from another in its pathological basis, a person of skill in the art would

not reasonably expect to treat the diseases with the same therapeutic agent and achieve the same result. This is further supported by post-filing publications that demonstrate that the anti-IL-8 antibody treatment in direct injury reverses the lung damage directly caused by the acid, *i.e.*, alveolar epithelium injury. *See, e.g.,* Exhibit B. In this publication, the administration of the anti-IL-8 antibody immediately before injecting the acid modulated the effects of the acid on the lung injury. However, it is not immediately apparent that such an administration would have any impact whatsoever on indirect injury which takes days to develop and typically has other complicating factors such as sepsis, nor is such an extrapolation suggested. Thus, while the use of the anti-IL-8 antibody may be obvious to try in indirect lung injury, it fails to provide a reasonable expectation of success for anti-IL-8 antibody in the treatment of indirect injury at the time of filing.

In view of the above, the basis for the rejection may be removed.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding objections and rejections of the claims and to pass this application to issue.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 350292000500. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: April 6, 2005

Respectfully submitted,

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